

Docket/App No.: 1242.1015-009  
Title: Short Peptides Which Selectively....  
Inventor: Shmuel A. Ben-Sasson

1      2      3      4      5      6      7      8      9      10  
Y/F    X    L/M    L/M/A/I    X    G/A    X    Hydrophobic    P    F/Y

Figure 1

1      2      3      4      5      6      7      8      9      10  
Y    E    M    L/M/A    X    G    X    P    P    F  
  
11    12    13    14    15    16    17    18    19    20  
X    A/G    D/E/Q    D/E/Q/N    P/E    D/E/I    D/E/Q    I/L    Y/F    Q/E

Figure 2

SERINE\THREONINE KINASES

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
RAF	Y	E	L	M	T	G	H	L	P	Y	S	H	I	N	N	R	D	Q	I	I
	F	Q	I	V	A	A	Q	D	F	A	N	L	D*	D*	X	D	E	L	L	
	W	E*	M	L	S		D	M	W	T	D	M	D	D*	E*	D	E*	M	M	
		N	V	I			E*	V			Q	V	E	E*	E*	E*	N	V	V	
		D					D*				E		E*	E*		D	D*	D		
		D*																		
CAPK	Y	E	M	A	A	G	Y	P	P	F	F	A	D	Q	P	I	Q	I	Y	E
	F	Q	V	G	V	A	F			Y	Y	G	N	E*		L	L	F	F	*
	W	E*	L	M	L	M	W			W	W		D*	E*		M	E*	M	M	W
		D	I	I	L	I							Q	N		V	N	N	N	*
		D*											E*	D*		D	D*	D	D*	
		N											E*	D*		D	D*	D	D*	
PKC	Y	E	M	L	A	G	Q	P	P	F	D	G	E	D	D	E	D	L	F	Q
	F	Q	V	M	I	C	H			Y	E	A	N	Q	N	Q	E	I	Y	H
	W	E*	L	I	V	L	E			W	H		D*	E*	D*	N	Q	M	M	*
		D	I			M	E				Q		E*	E*	E	N	Q	V	V	
		D*				V					N		D*	D*	D	D*	D	D*	D	
		N									E*					E*				
BARK1.2	F	K	L	I	R	G	H	S	P	F	R	Q	H	K	T	K	D	K	H	E
	Y	O	I	L	X	A	T	T	Y	W	X	O	O	O	S	O	N	O	O	O
	W	M	M	M	V	V						D	D	D			Q	Q	Q	Q
		V	V	V	V	V						N	E*	E*			E*	E*	E*	E*
												E*	D*	D*	E*	D				
CaMK	Y	I	L	L	V	G	Y	P	P	F	W	W	D	N	E	D	N	R	Y	Q
	F	L	I	I	L	A	F			Y	Y	F	Q	Q	Q	E	E	K	F	H
	W	M	M	M	M	C	W			W	W	F	D*	D*	D*	D*	D*	M	M	*
		V	V	V	V	I						E*	D*	D*	E*	D		V	V	

Figure 3A

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
POLO	Y	T	L	L	V	G	K	P	P	F	E	T	S	C	L	K	E	T	Y	L
	F	S	M	I	L	A	R			Y	D	S	T	T	V	O	D	S	F	I
	W	I	M	I	O				W	Q	N			S	I	N	Q	W	V	M
		V	V	M		X				N	E*			M		E*	D*			
										E*										
										D*										
Akt / PKB	Y	E	M	M	C	G	R	L	P	F	Y	N	Q	D	H	E	R	L	F	E
	F	E*	L	L	S	A	X	M	W	W	Q	Q	N	D*	K	E*	X	M	Y	E*
	W	D	I	I	T			I	Y	F				E*	O	D	K	I	W	D
		D*	V	V				V							E*	D	V		D*	
GRK1	Y	E	M	I	A	A	R	G	P	F	R	A	R	G	E	K	V	N	Q	K
	W	E*	I	M	G	G	X	A	W	W	X	G	X	A	E*	O	M	I	D	O
	F	D	L	L					Y						D	H	H	L	D	H
	D*	V	V												D*	D	D	D*		
GRK4	Y	E	M	I	Q	G	H	S	P	F	K	K	Y	K	E	K	V	K	W	E
	F	E*	I	L	N	A	K	T	W	Y	O	O	F	O	E*	O	M	O	F	E*
	W	D	L	M	O				Y	H	H	W	H	H	D	H	I	H	Y	D
	D*	V	V												D*	H	L		D	D*
GRK5	Y	E	M	I	E	G	Q	S	P	F	R	G	R	K	E	K	V	K	R	E
	F	E*	I	L	E*	A	N	T	W	X	A	X	X	O	E*	O	M	O	X	E*
	W	D	L	M	D				Y					H	D	H	I	H		D
	D*	V	V		D*										D*	L				D*
GRK6	Y	E	M	I	A	G	Q	S	P	F	Q	N	R	K	K	K	I	K	R	E
	F	E*	I	L	G	A	N	T	W	Y	Y	Y	X	O	O	O	M	O	X	E*
	W	D	L	M										H	H	H	H	V	H	D
	D*	V	V														L		D	D*
GSK3	A	E	L	L	L	G	Q	P	I	F	P	G	D	S	G	V	D	Q	L	V
	G	E*	I	I	I	A	N		L	Y	A	D*	T	A	L	D*	N	I	I	L
	D	M	M	M					M	W	E		E		I	E	M	M	I	M
	D*	V	V	V					V		E*				M	E*		V	M	M

D\* = a substituted or unsubstituted aliphatic, benzylic or aromatic ester of aspartic acid

E\* = a substituted or unsubstituted aliphatic, benzylic or aromatic ester of glutamic acid

X = N-nitroarginine,  $\beta$ -cycloarginine,  $\gamma$ -hydroxyarginine, amidinocitroline or 2-amino-4-guanidinobutanoic acid

O = Ornithine

Figure 3B

RAE

HJ38	Ac-	V	M	T	G	Q	L	P	F	-NH <sub>2</sub>
J41	Ac-	V	M	T	G	E!	L	P	F	-NH <sub>2</sub>

POLO

J42	Ac-	M	L	L	G	R	P	P	F	E!	-NH <sub>2</sub>
J43	Ac-	M	L	L	G	K	P	P	F	NH <sub>2</sub>	
J43.1	Ac-	M	L	L	G	K	P	P	F	E!	-NH <sub>2</sub>
J45			Ac-	L	G	R	P	P	F	E!	T S
J46	Ac-	M	L	L	G	R	P	P	F	E!	T S
											-NH <sub>2</sub>

AkT/PKB

J47				Ac-	G	R	L	P	F	F	N	-NH <sub>2</sub>
J48	Ac-	E!	M	M	G	R	L	P	F	F	N	-NH <sub>2</sub>

GSK3

J29	Ac-	L	L	L	G	Q	P	I	F	P	G	-NH <sub>2</sub>
-----	-----	---	---	---	---	---	---	---	---	---	---	------------------

E! - Benzyl Ester of Glutamic Acid

Figure 4

Collagen production in fetal lung fibroblasts  
in the presence of increasing concentrations of  
K048H101

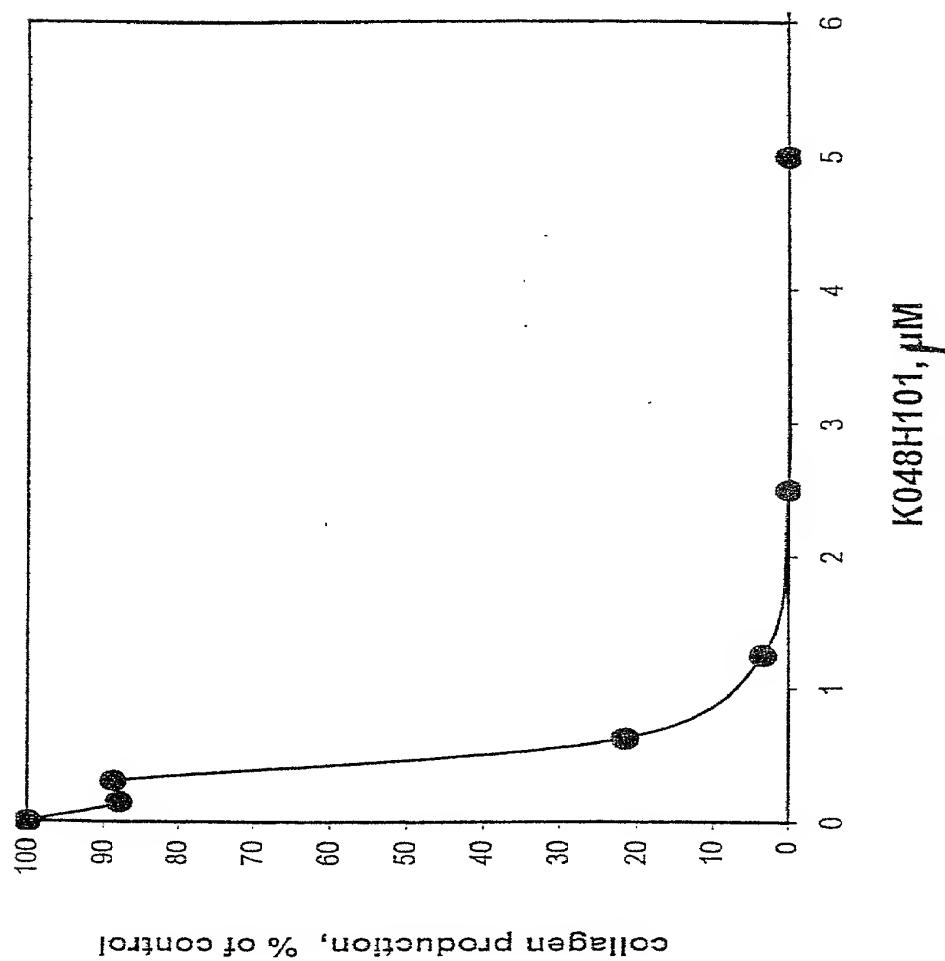


Figure 5

Activin/TGFbR  
ACTRII

	<b>Peptide N_terminal</b>		<b>C_terminal</b>
	K095H101 Myristyl - G	G P V D E Y M L P F	NH2

ALK1

	<b>Peptide N_terminal</b>		<b>C_terminal</b>
	K048H101 Myristyl - G	G I V E D Y R P P F	NH2
	K048H901 Stearyl - G	G I V E D Y R P P F	NH2

ALK3

	<b>Peptide N_terminal</b>		<b>C_terminal</b>
	K098H101 Myristyl - G	G I V E E Y Q L P Y	NH2
	K098H901 Stearyl - G	G I V E E Y Q L P Y	NH2

ALK4

	<b>Peptide N_terminal</b>		<b>C_terminal</b>
	K099H101 Myristyl - G	G Q V H E E Y Q L P Y	NH2

TGFbRII

	<b>Peptide N_terminal</b>		<b>C_terminal</b>
	K093H101 Myristyl - G	G E V K D Y E P P F	NH2

Akt/PKB  
Akt1/Raca

	<b>Peptide N_terminal</b>		<b>C_terminal</b>
	K014H101 Myristyl - G	M M S G R L P	NH2
	K014H010 (Free NH2)	M C G R L P	NH2
	K014H111 Myristyl - G	M M C G R L P	NH2

CAPK  
cAPKa

	<b>Peptide N_terminal</b>		<b>C_terminal</b>
	K004H001 Acetyl	M A A G Y P	NH2
	K004H002 Acetyl	M A A G Y P P F F	NH2

CDK

Figure 6A

CDK2

Peptide N_terminal		C_terminal
K049H101	Myristyl - G	M V T R R A L F

CDK4

Peptide N_terminal		C_terminal
K050H101	Myristyl - G	M F R R K P L F

CHK  
Chk1

Peptide N_terminal		C_terminal
K088H001	Acetyl	M L A G E! L P W D!
K088H101	Myristyl -G	M L A G E L P
K088H103	Myristyl - G	M L A G E L
K088H104	Myristyl - G	M L A G E L P W D

DAPK  
DAPK

Peptide N_terminal		C_terminal
K092H001	Acetyl	I L L S G A S P F L G

GRK  
bARK1

Peptide N_terminal		C_terminal
K024H101	Myristyl - G	L L R G H S

GSK3  
GSK3b

Peptide N_terminal		C_terminal
K018H101	Myristyl - G	L L L G Q P I

IAK  
Iak1

Peptide N_terminal		C_terminal
K087H001	Acetyl	F L V G M P P F
K087H101	Myristyl -G	F L V G M P P
K087H102	Myristyl -G	F L V G M P

Figure 6B

IKK K087H103 Myristyl -G F L V G M P P F E NH2  
IKK-1

---

Peptide N\_terminal C\_terminal  
IKK-2

---

K090H101	Myristyl - G	I A G Y R P F L	NH2
----------	--------------	-----------------	-----

---

Peptide N\_terminal C\_terminal  
ILK K091H001 Acetyl I T G F R P F L NH2  
ILK K091H101 Myristyl -G I T G F R P F L NH2

---

Peptide N\_terminal C\_terminal  
MARK/p78  
MARK1

---

K107H001	Acetyl	L V T R E! V	NH2
K107H101	Myristyl -G	L V T R E V P F	NH2
K107H102	Myristyl - G	L V T R E V	NH2
K107H901	Stearyl - G	L V T R E V P F	NH2

---

Peptide N\_terminal C\_terminal  
PKC K045H101 Myristyl -G L V S G S NH2  
PKCb K045H102 Myristyl -G L V S G S L P NH2

---

Peptide N\_terminal C\_terminal  
K008H001 Acetyl M L A G Q A P F NH2  
K008H101 Myristyl -G M L A G Q A P NH2  
K008H102 Myristyl -G M L A G Q A NH2  
K008H103 Myristyl -G M L A G Q A P F E NH2

Figure 6C

POLO  
Plk

---

Peptide N_terminal		C_terminal	
K035H001	Acetyl	L L V G K P P F	NH2
K035H101	Myristyl -G	L L V G K P P	NH2

SNK

---

Peptide N_terminal		C_terminal	
K038H101	Myristyl -G	M L L G R P P F E!	NH2
K038H102	Myristyl -G	M L L G R P P	NH2

RAF  
Braf

---

Peptide N_terminal		C_terminal	
K003H103	Myristyl -G	L M T G Q L	NH2
K003H104	Myristyl -G	L M T G Q L P Y S	NH2

c-Raf

---

Peptide N_terminal		C_terminal	
K001H102	Myristyl -G	L M T G E L	NH2
K001H103	Myristyl -G	L M T G E L P Y S	NH2

Figure 6D